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(54) **RECONFIGURABLE SURFACE ENHANCED RAMAN SPECTROSCOPY DEVICE AND METHOD THEREFOR**

(58) **Field of Classification Search**
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See application file for complete search history.

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U.S. PATENT DOCUMENTS

6,558,956 B1 5/2003 Carron et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

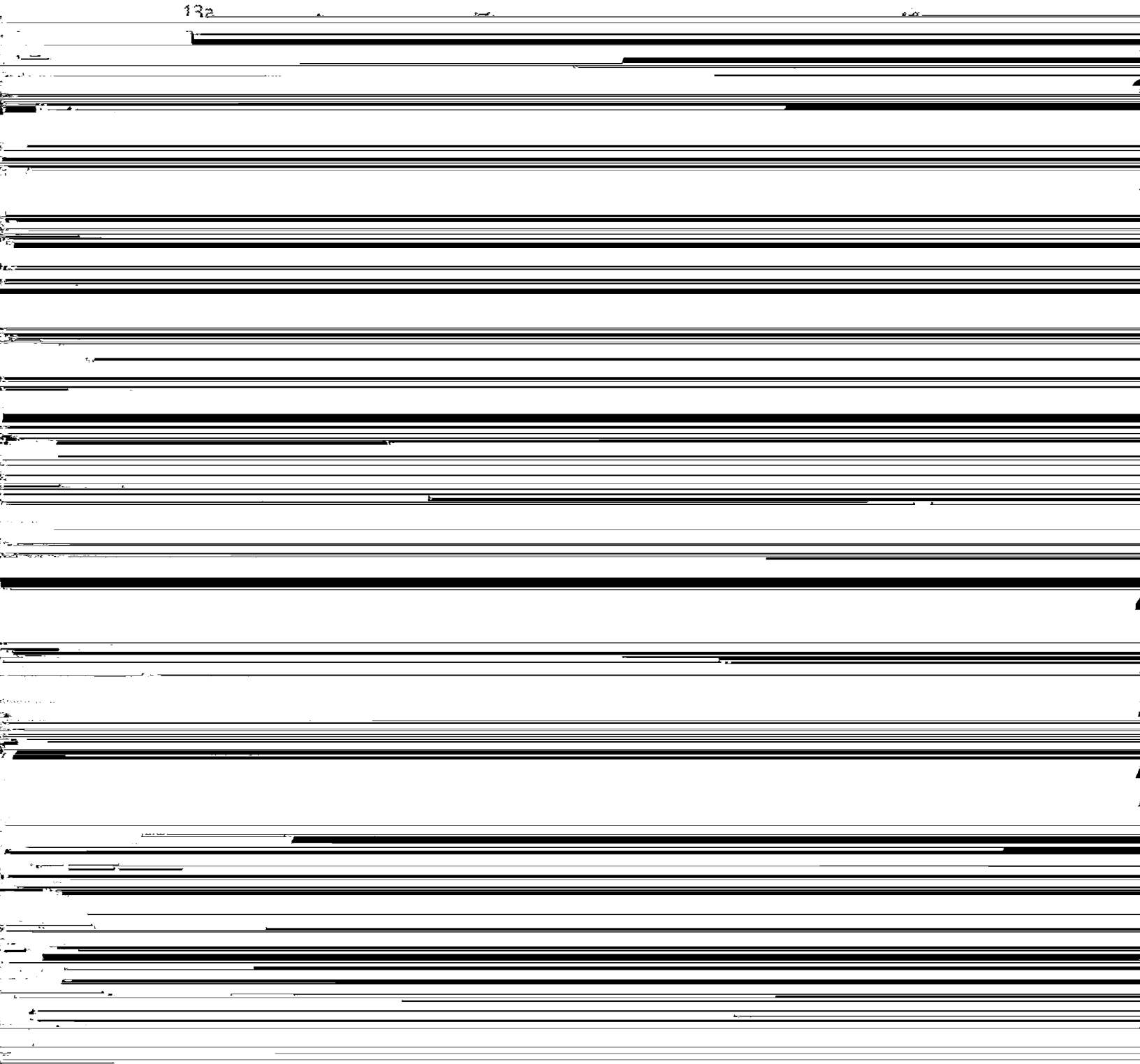
7,688,440 B2 3/2010 Clarke et al.
8,792,095 B2 * 7/2014 Piorek G01N 33/0057

9,255,842 B2 2/2016 Gardner et al.
10,001,443 B2 6/2018 Gardner et al.
2010/0040979 A1 2/2010 Weimer

Kim, M-S., et al., "Controlled Aggregation of Silver Nanoparticles Using DEP Force for SERS (Surface Enhanced Raman Spectroscopy) Analysis", IEEE Transducers The 13th International Confer-

Cheng, I-F., et al., "Rapid identification of bacteria utilizing amplified dielectrophoretic force-assisted nanoparticle-induced surface-

9, pp. 1-8, (2014).
Dies, H. et al., "In situ assembly of active surface-enhanced Raman scattering substrates via electric field-guided growth of dendritic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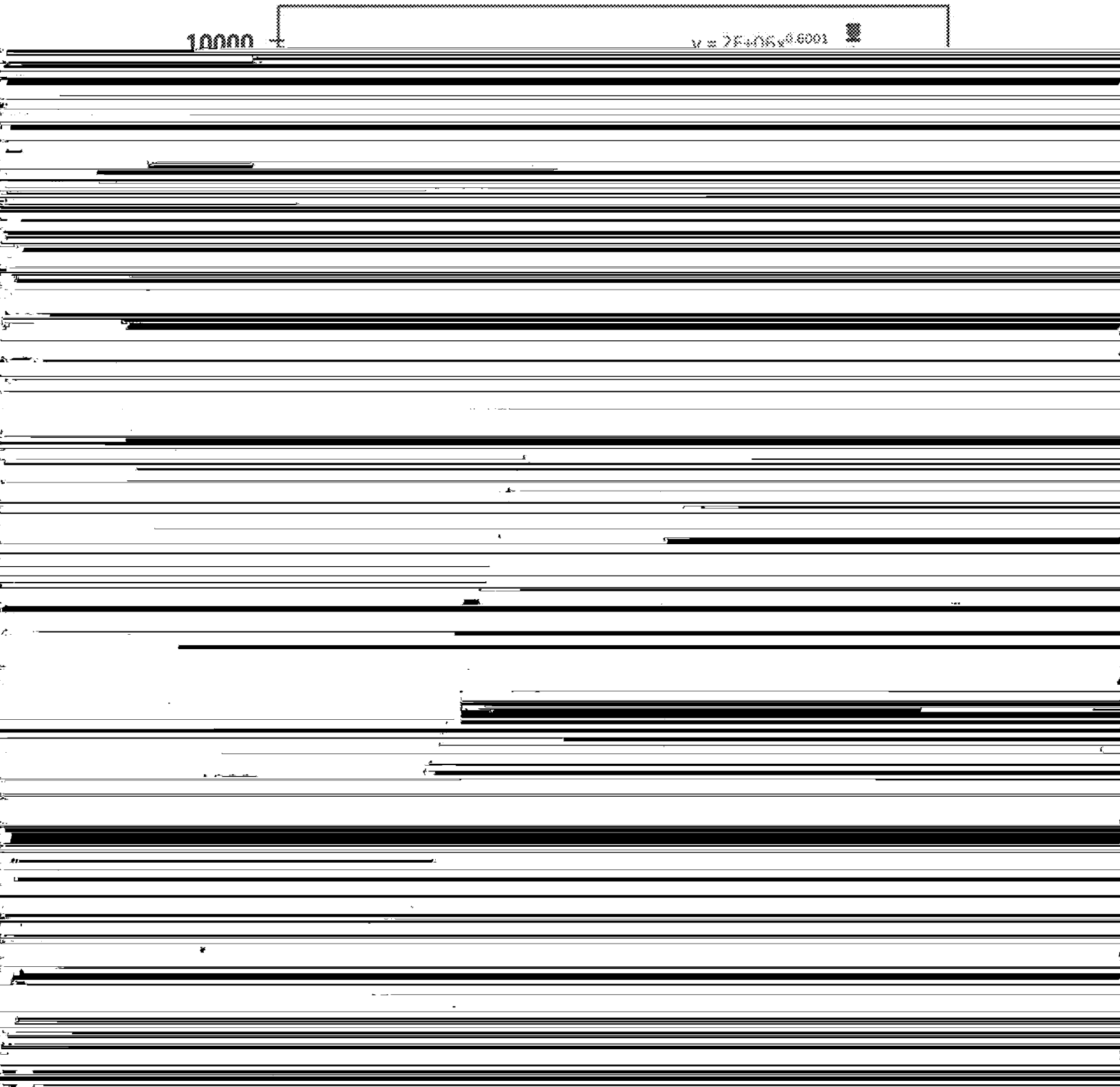

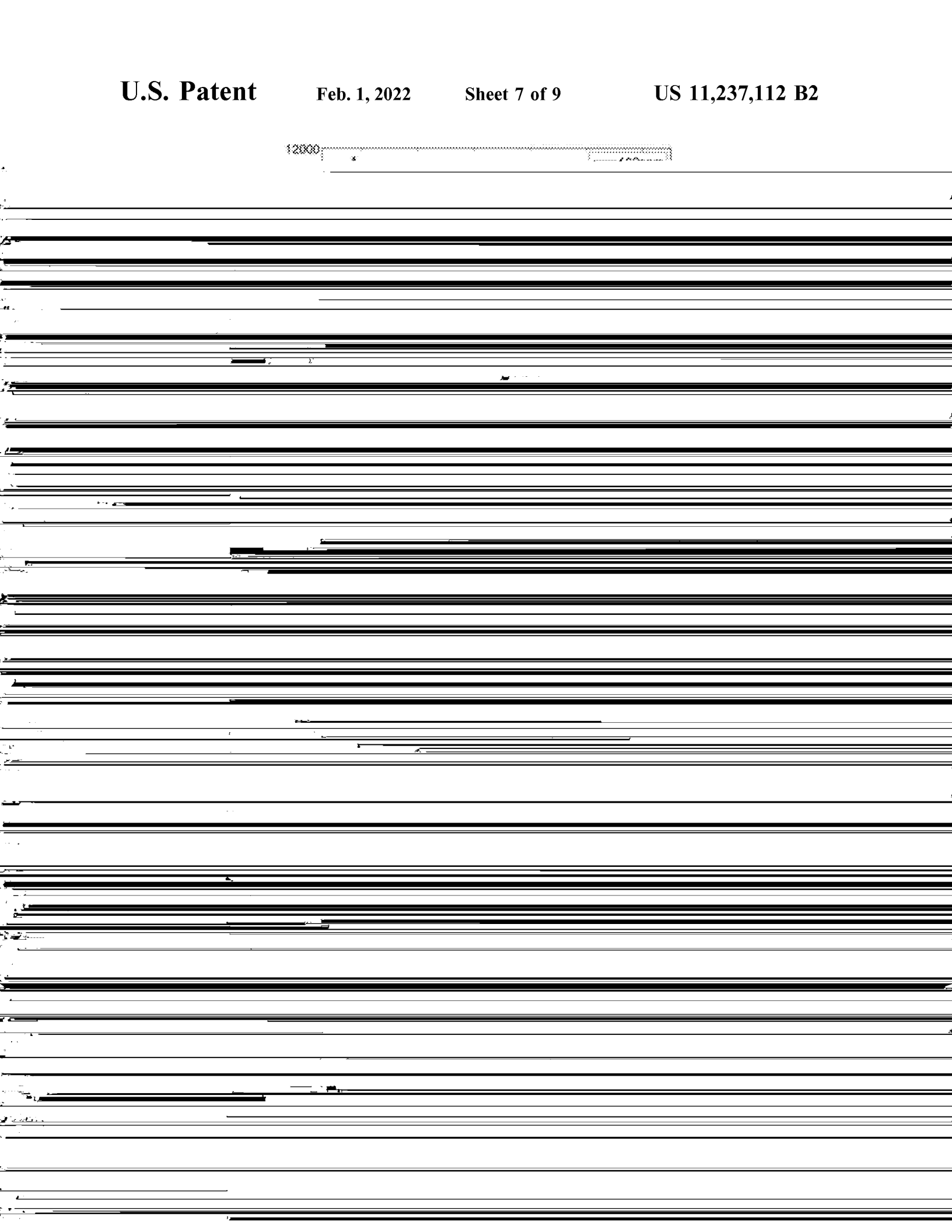
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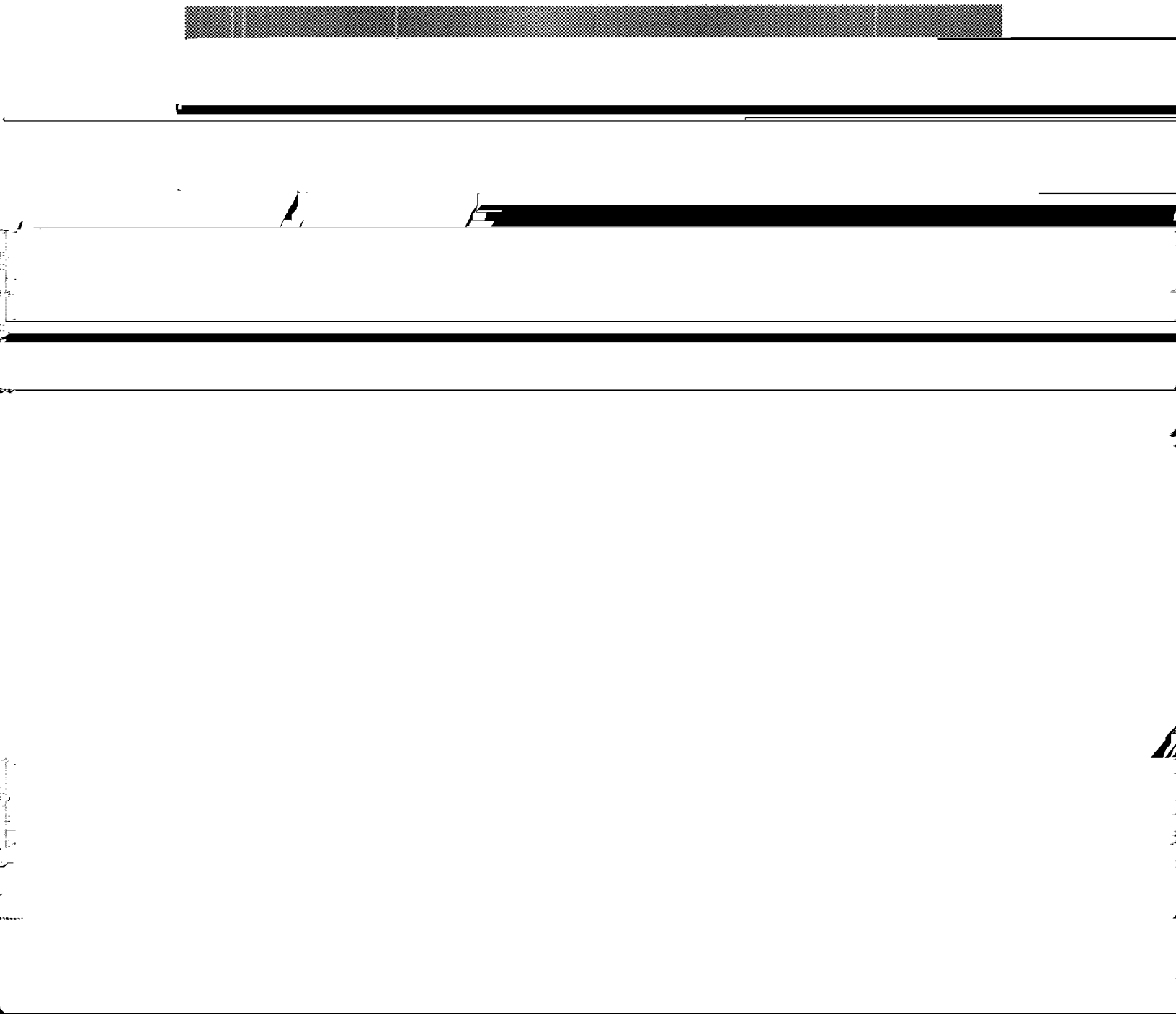

RECONFIGURABLE SURFACE ENHANCED RAMAN SPECTROSCOPY DEVICE AND METHOD THEREFOR

This application is a 371 of International Application No. PCT/CA2017/050931 flied on Aug. 4, 2017, and claims the benefit of the filing date of U.S. Application No. 62/373,537 filed on Aug. 11, 2016, the contents of which are incorpo-

substrate in a spaced relationship such that a detection site is formed along edges and/or between opposing edges of the microelectrodes; and a nanoparticle structure comprising a plurality of metallic nanoparticles disposed in the detection site.

Assembly of the nanoparticle structure may be directed by an electric field between the at least two microelectrodes. The electric field may comprise an AC electric field. The electric field may comprise an AC electric field with a DC

FIELD

This invention relates to surface enhanced Raman spectroscopy (SERS). More specifically, this invention relates to a highly sensitive SERS device that is simple and cost effective to produce, and re-usable.

field. The electric field may comprise an electrostatic field. The nanoparticle structure may be a branched, clustered, aggregated, fractal, and/or dendritic structure. In one embodiment, the nanoparticle structure is a dendritic structure.

The nanoparticles may be functionalized. The functionalized nanoparticles may include a surface modification. The

posed on the substrate in a spaced relationship such that a detection site is formed along edges and/or between opposing edges of the microelectrodes; disposing a plurality of metallic nanoparticles on the detection site under a condition

FIGS. **6**A, **6**B, and **6**C show results for melamine, cocaine, and thiram respectively, using passive surface adsorption of the analytes; all spectra represent averages from three different locations on the SERS device.

nanoparticles into a nanoparticle structure in the detection (FIG. **7**A) and *E. coli* K12 (FIG. **7**B) using a SERS device

of the device are arranged such that a 3-D electrode con-

trokinetic deposition comprises applying an alternating cur-

electrode(s) to be moved relative to the substrate electrodes. In another example, one or more electrodes may be disposed on a first substrate, and one or more electrodes may be disposed on a second substrate, and the first and second substrates arranged face-to-face (e.g., substantially co-planar, or at a selected angle) such that a 3-D electrode configuration is produced. The two or more microelectrodes may be deposited in their final form, or they may be formed, or their shape and/or size and/or spacing may be adjusted, by subsequently removing metal (e.g., by using a mechanical, chemical, laser, and/or micromachining technique). For example, the shape, size, and or spacing of the two or more microelectrodes may be carried out to adjust or tailor the size or shape of the detection site. Surface preparation of the solid substrate may be employed as necessary prior to depositing the metal, as would be apparent to one or ordinary skill in the art, to enable or enhance adhesion of the metal to the solid substrate.

As used herein, the terms "nanoparticle structure" and "nanostructure" refer to a structure that is assumed or

etc., to the two or more microelectrodes to generate an electric field between them (i.e., across the detection site). In some embodiments a direct current (DC) offset may also be applied to the two or more microelectrodes. In some embodiments a DC electric field or an electrostatic field may be applied to the two or more microelectrodes. The electric field acts on the nanoparticles to influence, induce, or direct formation of the nanoparticle structure, including, in some embodiments, the formation of branches, clusters and/or dendrites. The nanoparticle structure may be "active", which refers to the fact that characteristics of the structure, including the formation and extent of branches, clusters, and/or dendrites, may be controlled, tuned, and/or optimized during deposition as well as during analysis of a sample (i.e., dynamically) by providing and optionally controlling an electric field across an electrode gap. For example, an electric field may be controlled by adjusting one or more parameters (e.g., voltage, current, frequency, shape of waveform, duty cycle) of the AC current, and optionally the DC offset, to thereby adjust the electric field. Results show that

electrodes **12***a*, **12***b*, **13***a*, **13***b* (i.e., a quadrupolar micro-

Metallic dendritic nanostructures have been produced

[redacted]

[redacted] involving deposition and reduction from metal ion contain

urable. In this feature, embodiments contrast sharply with prior devices having soft substrates (e.g., paper in some prior devices). Because of the solid substrates, the dendrites may be removed (e.g., by washing with a simple surfactant solution, such as soap) from the surface after use, and

layer of chrome was used to improve the adhesion of the deposited Au layer (100 nm thickness) to the silicon substrate.

Analyte Sample Preparation

R6G was dissolved in methanol at a stock concentration

scope objective, 500 μm pinhole, 500 μm slit width. All

Raman spectra were background-corrected through polynomial subtraction, and noise was reduced with a Savitsky-Golay filter.

Optimization of Electrokinetic Nanoparticle Deposition

Optimization experiments were conducted across a wide

range of voltage and frequency conditions. A window for

dendrite formation was found to include a frequency of about 1-100 Hz, and a voltage of about 2.5-3.5 V peak-to-peak (i.e., an electric field intensity of about $1.5\text{-}2.1\times10^5$ V/m). For example, in one experiment, extended dendrites

submicron scale) and may be difficult to reproduce with standard photolithographic techniques. Therefore, this method of enhancing dendrite growth provides embodiments with small microelectrode gaps while avoiding the need for specialized production techniques or equipment,

FIG. **3** shows the results of optimization experiments conducted with embodiments using AgNPs and AuNPs, where SERS performance is quantified through the intensity of a key peak ($1360\ cm^{-1}$) in the Raman spectrum of

cocaine, and (3) thiram. Melamine is a nitrogenous industrial chemical used in resin production and fertilizer, which, upon ingestion and metabolization may form insoluble crystals in the kidney, leading to renal failure. Because of its high nitrogen content (66.7% by mass), melamine has been added to dairy products, infant formulations, or pet food, in order to boost the apparent protein content. Such use has resulted in the deaths of hundreds of cats and dogs in the United States in 2007, and the hospitalization of over 50,000 [illegible] in China in 2008. The World Health Organization

r^3) would only be capable of attracting large biological objects, such as bacteria and viruses. In the presence of a dendritic nanoparticle structure, however, this capability may be extended to smaller objects, such as biomolecules (e.g., proteins, DNA). To demonstrate the principal of active analyte concentration amplification here, the technique is applied to the detection of BSA, an abundant plasma protein, as well as *E. coli* K12, a Gram negative rod-shaped bacterium.

graphene-coated dendrites (upper trace). Overall, 2- to 5-fold SERS signal enhancement was observed

electrode configuration is provided and a detection site is formed along edges and/or between opposing edges

INCORPORATION BY REFERENCE

All cited publications are incorporated herein by reference in their entirety.

EQUIVALENTS

of the first and second electrodes; and

disposing a plurality of metallic nanoparticles on the detection site under a condition that induces, directs, or influences assembly of the metallic nanoparticles into a nanoparticle structure in the detection site along edges and/or between opposing edges of the first and second electrodes in the absence of an analyte;

wherein the nanoparticle structure comprises at least one

26. The method of claim **9**, wherein the second electrode is disposed on the first non-electrically conductive substrate;

wherein a 2-D electrode configuration is provided.

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